Crystal Structure of Stem Cell factor: Implication In Stem Cell Factor Receptor Dimerization and Activation

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Introduction: Stem cell factor (SCF) plays important roles in hematopoiesis and the survival, proliferation, and differentiation of mast cells, melanocytes, and germ cells. SCF mediates its biological effects by binding to and activating a receptor tyrosine kinase designated c-kit or SCF receptor.

Methods and Materials: Recombinant human stem cell factor is crystallized in the presence of Sm ions, in space group P21. The crystals diffract to better than 2 Å resolution. X-ray diffraction data at 1.03 Å and 1.55 Å were collected. MAD phasing was used to solve the structure. Final model was refined to 2.3 Å resolution.

Results: We determined a 2.3 Å crystal structure of the functional core of recombinant human SCF. SCF is a noncovalent homodimer composed of two slightly wedged protomers (Fig. 1). Each SCF protomer exhibits an antiparallel four-helix bundle fold. Dimerization is mediated by extensive polar and nonpolar interactions between the two protomers with a large buried surface area. Finally, we have identified a hydrophobic crevice and a charged region at the tail of each protomer that functions as a potential receptor-binding site. On the basis of these observations, a model for SCF·c-kit complex formation and dimerization is proposed.

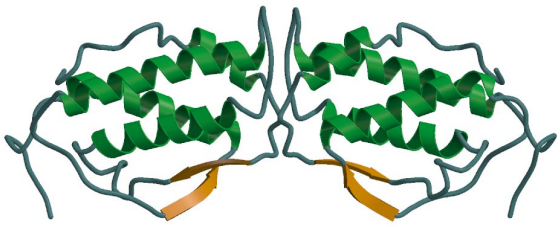

Fig. 1 Overall structure of SCF dimmer in ribbon representation.

References: Z. Zhang et al., PNAS **97**, 7732 (2000).